昆明醫科大學
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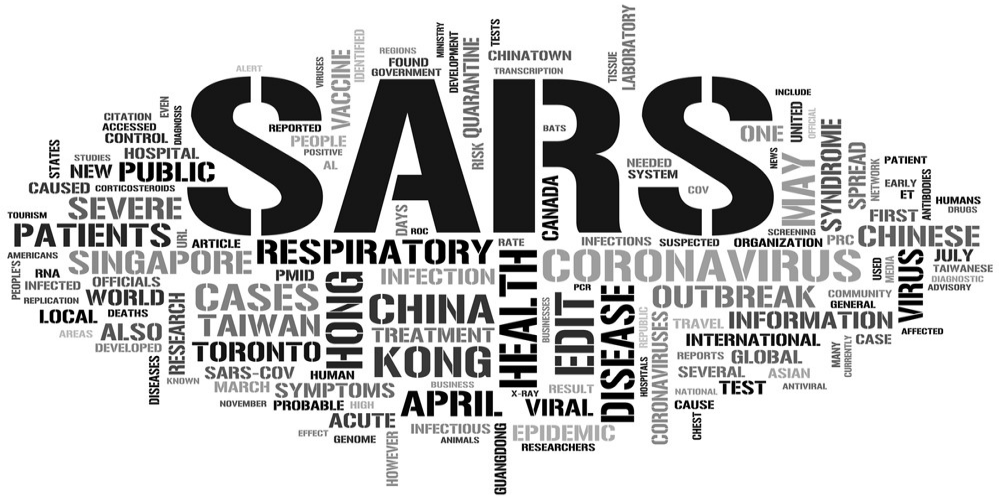
Infectious pathogens —

Molecular detection of virus infections

Prof. Dr. Feng Hui

School of Medicine, Chongqing University

YEAR 2003


SARS
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TAIWAN
TORONTO
SINGAPORE
PATIENTS
SEVERE
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REPORTED
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QUARANTINE
CHINATOWN
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NETWORK
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EARLY
ET
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DRUGS
FIRST
CHINESE
JULY
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DIAGNOSTIC
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VIRAL
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RESEARCHERS
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SEVERAL
REPORTS
GLOBAL
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INTERNATIONAL
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ALERT
VIRUSES
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OFFICIAL
NEWS
ANTIBODIES
TOURISM
URL
DISEASES
CORONAVIRUSES


抗击非典


一个国家 一个民族 一个城市 一个家庭
战胜"非典
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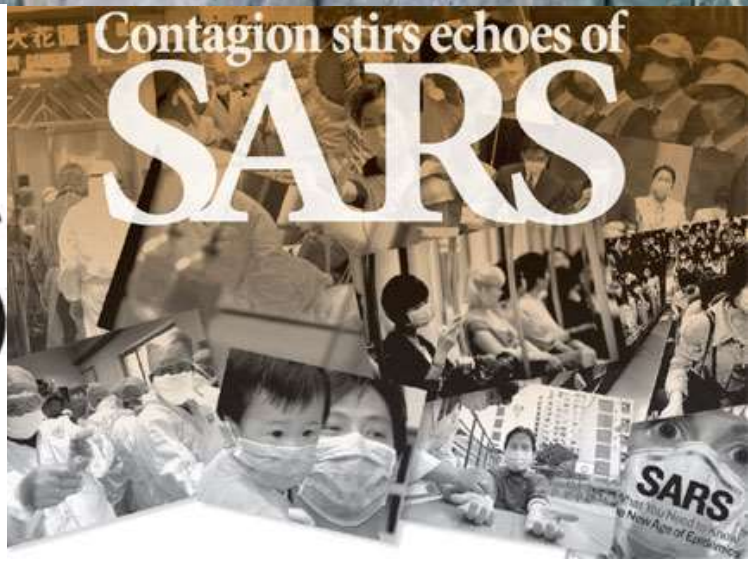
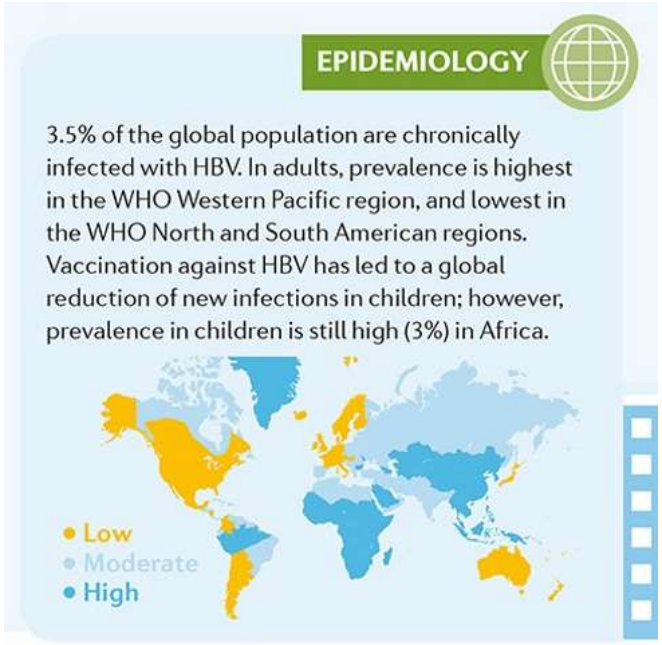
SARS
TodayOnHistory.com

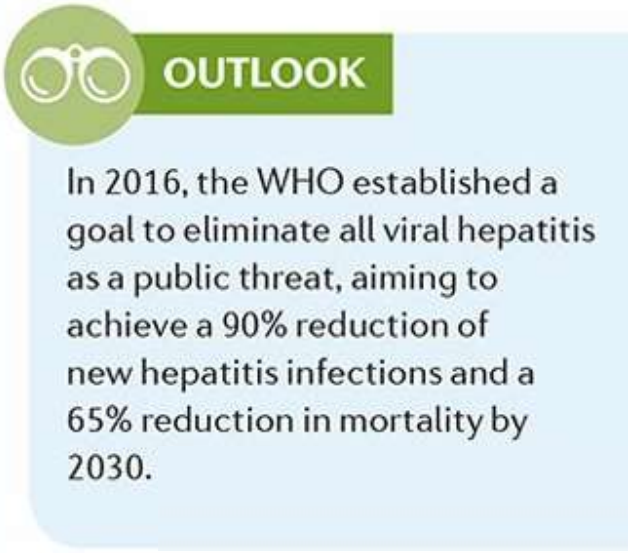

Contagion stirs echoes of
SARS
SARS

Wuhan Institute of Virology: Hepatitis B

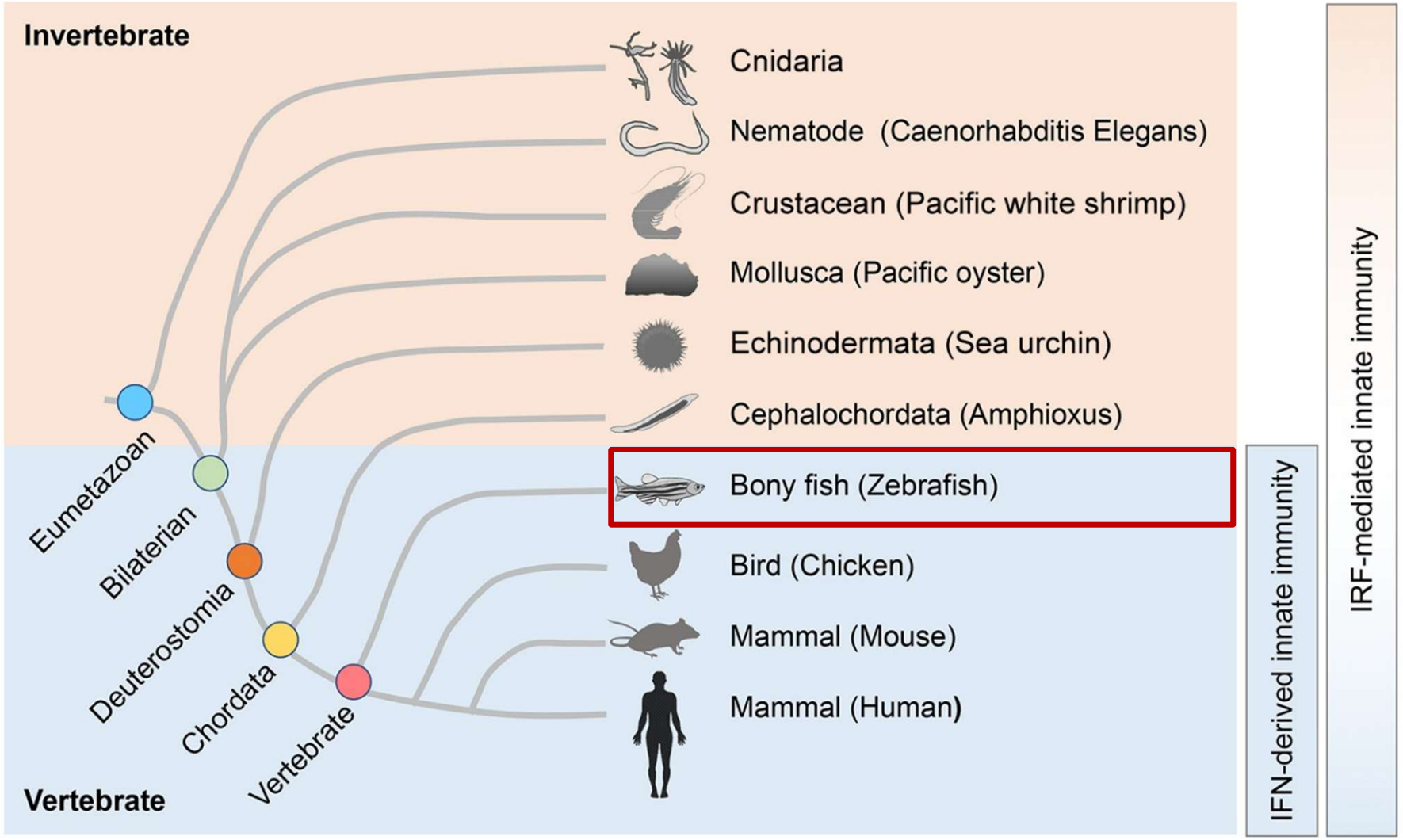
remains a pervasive global health challenge, affecting an estimated **254 million** people worldwide

- A disease that caused by a small DNA virus: hepatitis B virus
- Can be a lifelong chronic disease
- Without treatment, patients have a high risk to develop liver fibrosis, cirrhosis and hepatocellular carcinoma



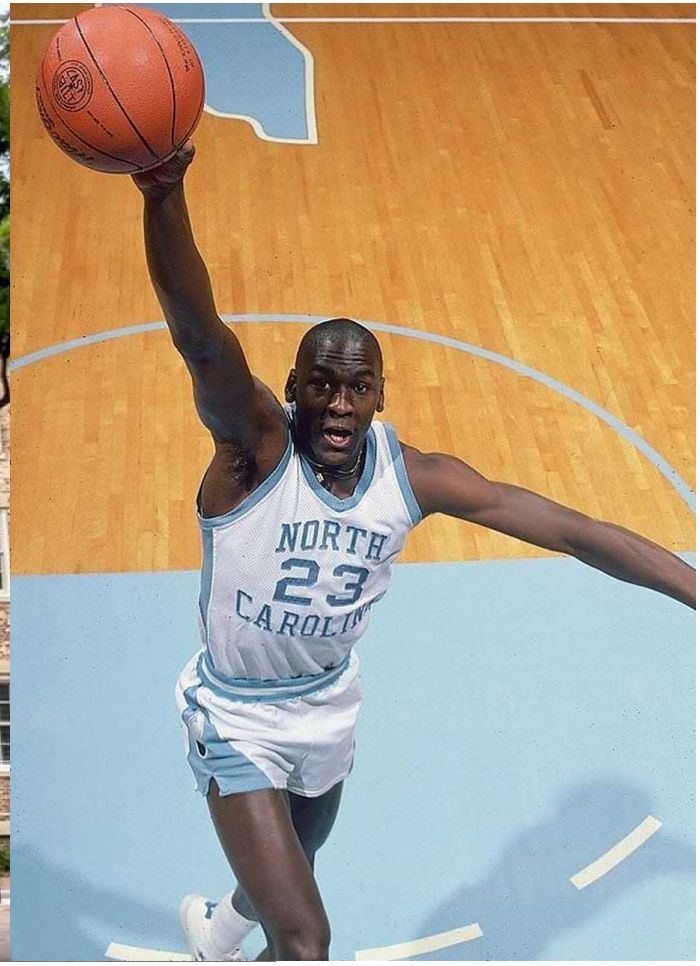


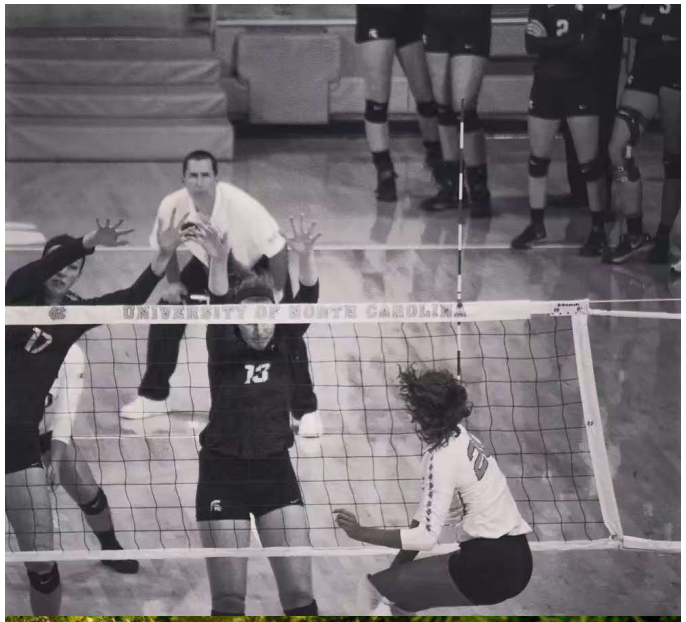
Institute of Hydrobiology: Innate immunity in zebrafish



UNC-Chapel Hill



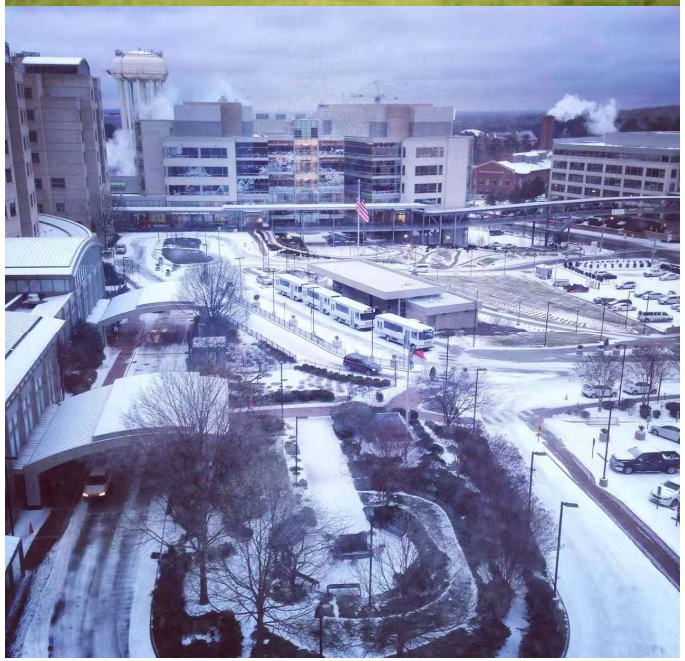



UNIVERSITY OF NORTH CAROLINA
13



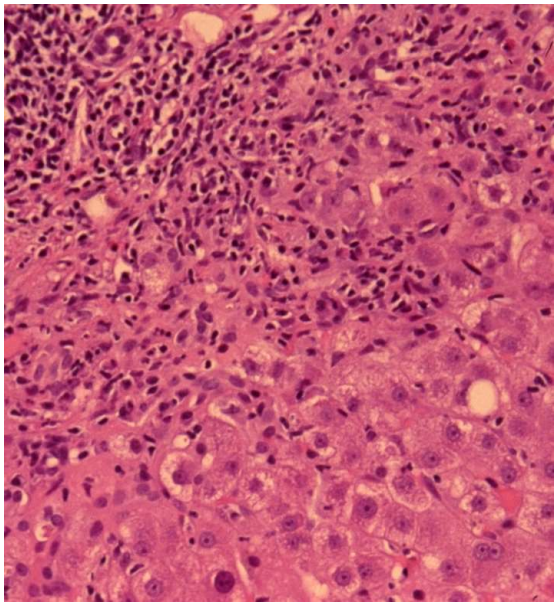

NORTH CAROLINA
UNIVERSITY OF
7


Carolina Families



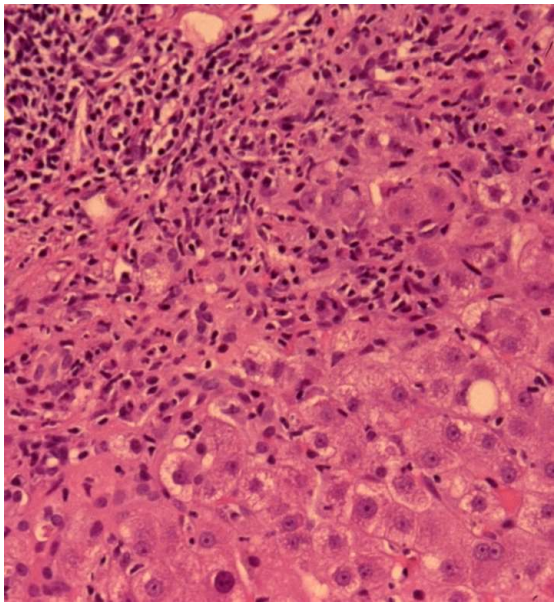


UNC-Chapel Hill: Hepatitis A



- Fecal-orally transmitted acute viral hepatitis
- Point-source and person-to-person spread
- Incubation period ~30 days (range 15-50)
- Chronic sequelae: none or extremely rare
- Complications: Fulminant/fatal hepatitis
  Relapsing hepatitis A
  Prolonged cholestasis

Hepatitis A



SEARCH

Los Angeles Times

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CALIFORNIA · U.S. & WORLD LOCAL ENTERTAINMENT SPORTS POLITICS OPINION MOST POPULAR PLACE AN AD TUESDAY OCTOBER, 17, 2017

Death toll from San Diego hepatitis A outbreak rises to 19; more than 500 cases confirmed



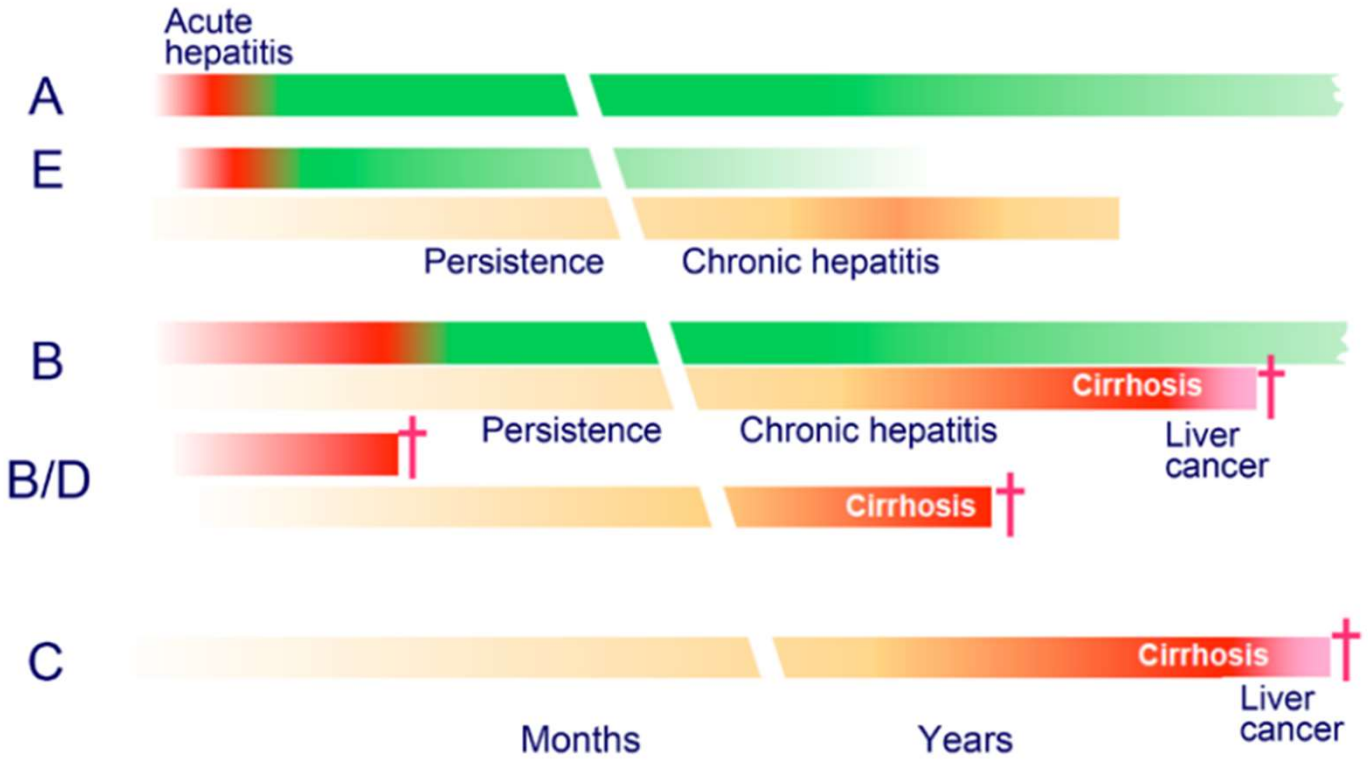
Work crews spray a bleach solution at North Park Community Park on Oct. 13 as part of the battle against the hepatitis A outbreak in San Diego. (Eduardo Contreras / San Diego Union-Tribune/TNS)

By Paul Sisson

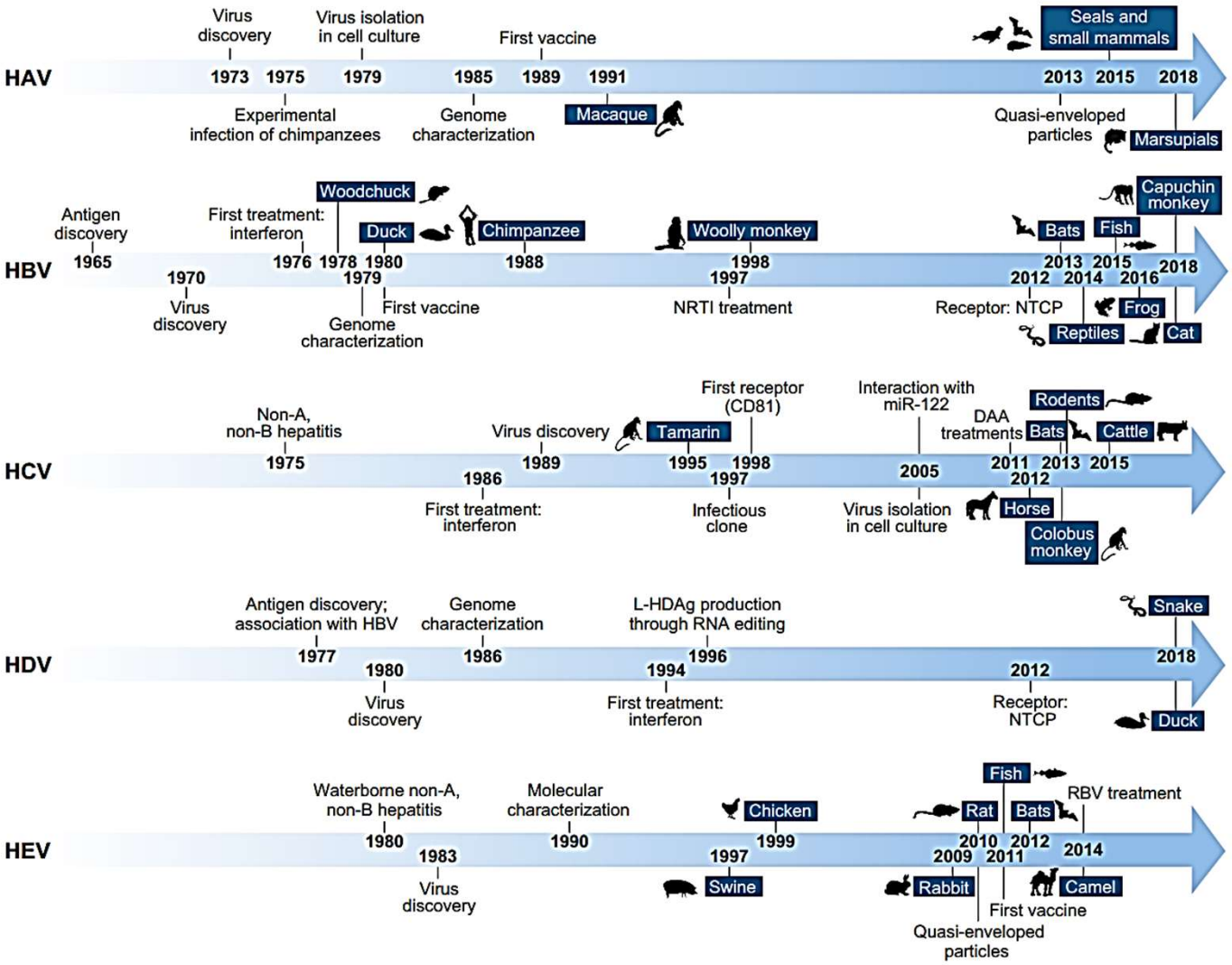
San Diego's hepatitis A outbreak added another death Tuesday, pushing the total to 19 as the number of confirmed cases passed 500.

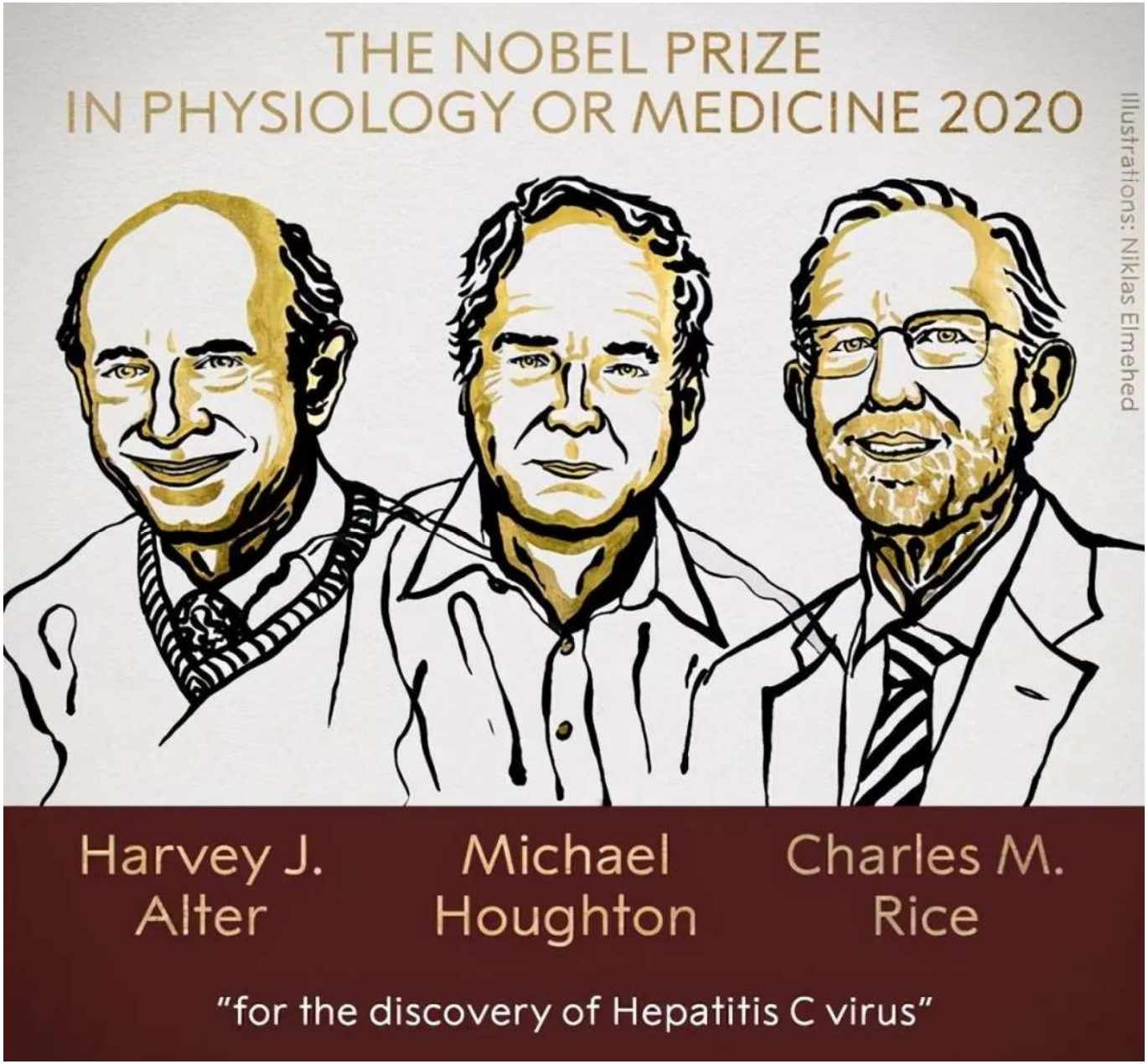
Updated numbers released by the county Health and Human Services Agency come as a massive effort around vaccination, sanitation and public education continues to try and stop the largest surge of the viral disease since the vaccine for hepatitis A was

The spectrum of human hepatitis viruses



Selected milestones in hepatitis virus research

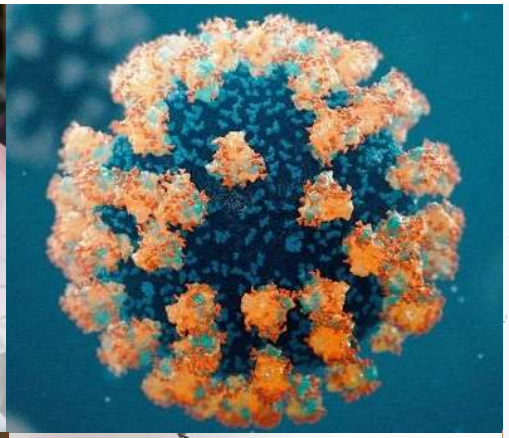



THE NOBEL PRIZE
IN PHYSIOLOGY OR MEDICINE 2020
Illustrations: Niklas Elmehed
Harvey J. Alter
Michael Houghton
Charles M. Rice
"for the discovery of Hepatitis C virus"

Viruses are going VIRAL

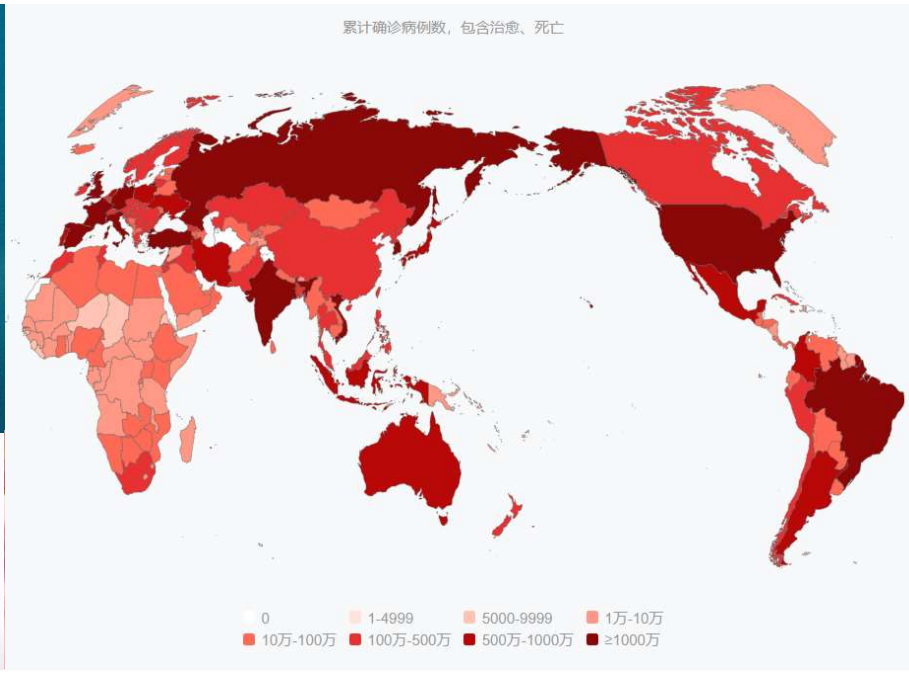
From 2003 to 2020：SARS, H7N9, H5N1, Ebola, Zika, Dengue, COVID-19…











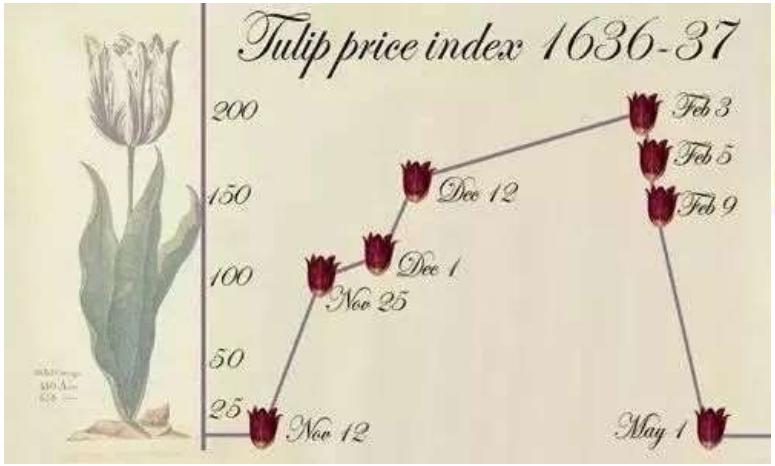
Discussion

- Where are you from?
- Have you encountered or are you aware of any diseases associated with viral infections?
- What is a virus?
- How viruses work?
- Are viruses all bad?

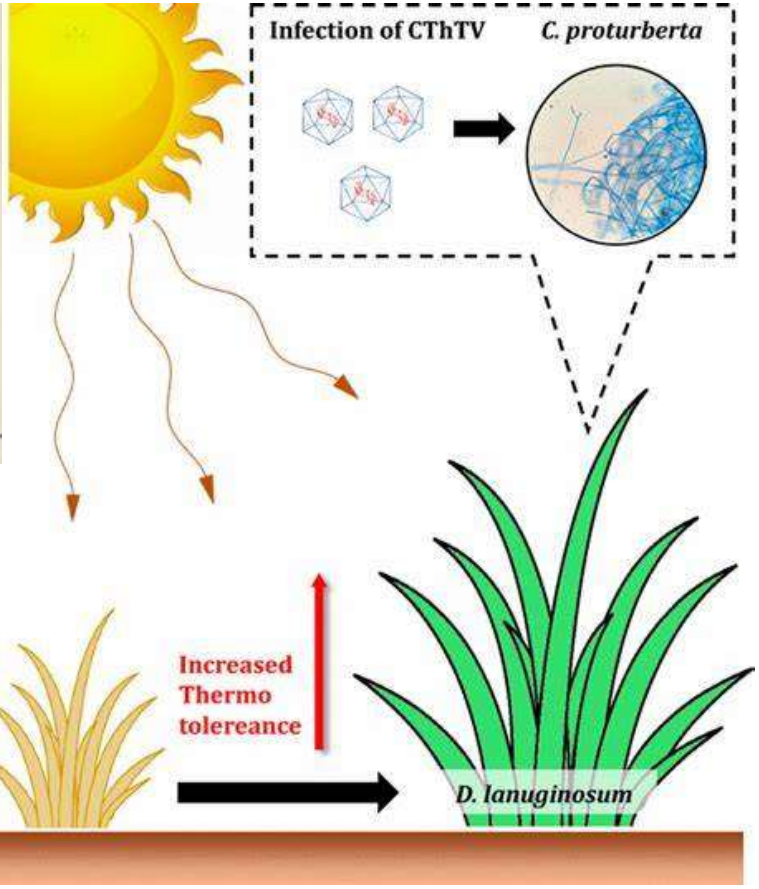
Viruses： The Good, the Bad and the Ugly



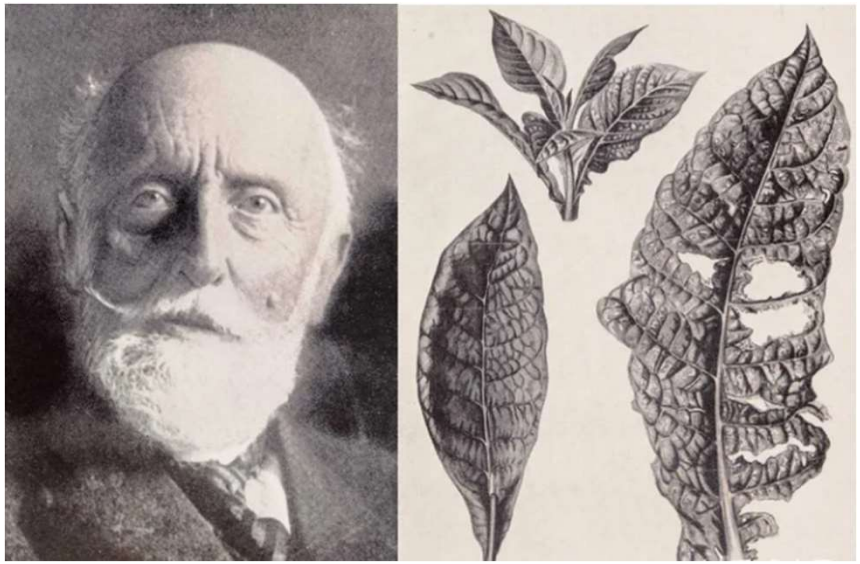
Tulip breaking virus







How Were Viruses Discovered?



Dmitri Ivanovsky (1892)

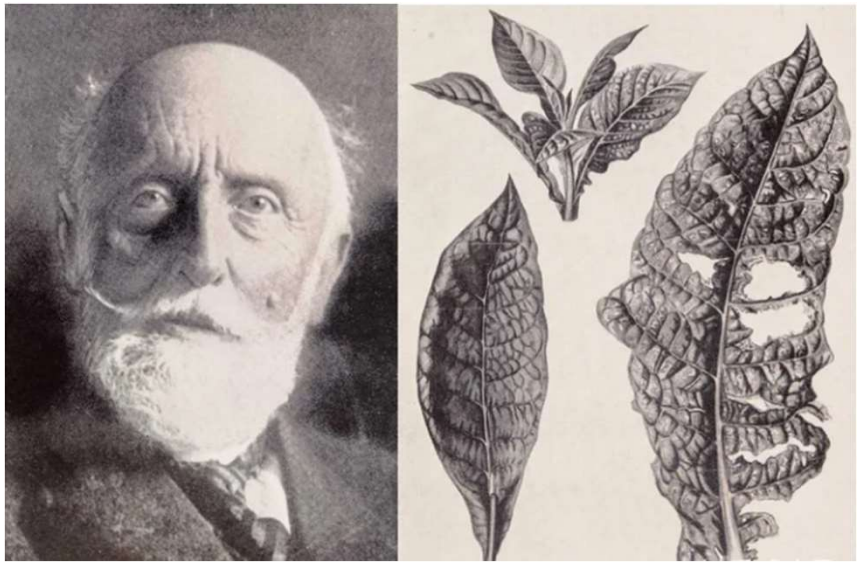


“filterable virus”



Dutch microbiologist and botanist Martinus W. Beijerinck (1898)

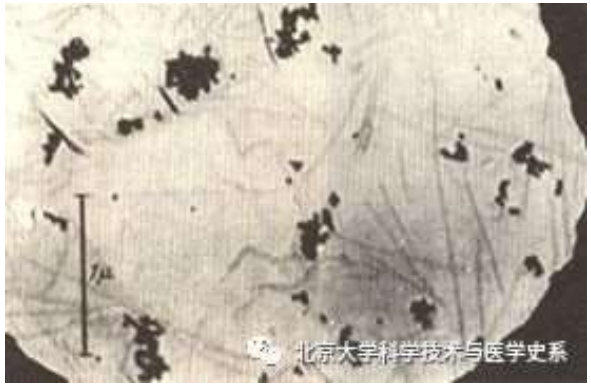
How Were Viruses Discovered?



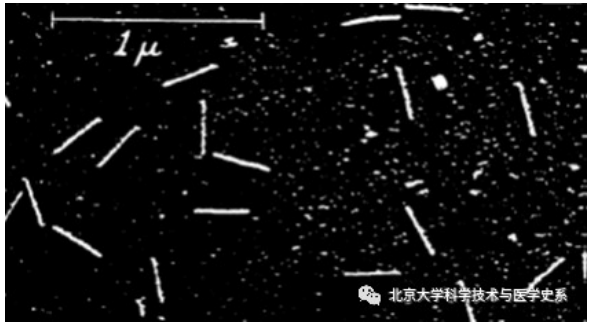
Dmitri Ivanovsky (1892)

Ernst Ruska & Bodo von Borries (1933)
The first Electron Microscope





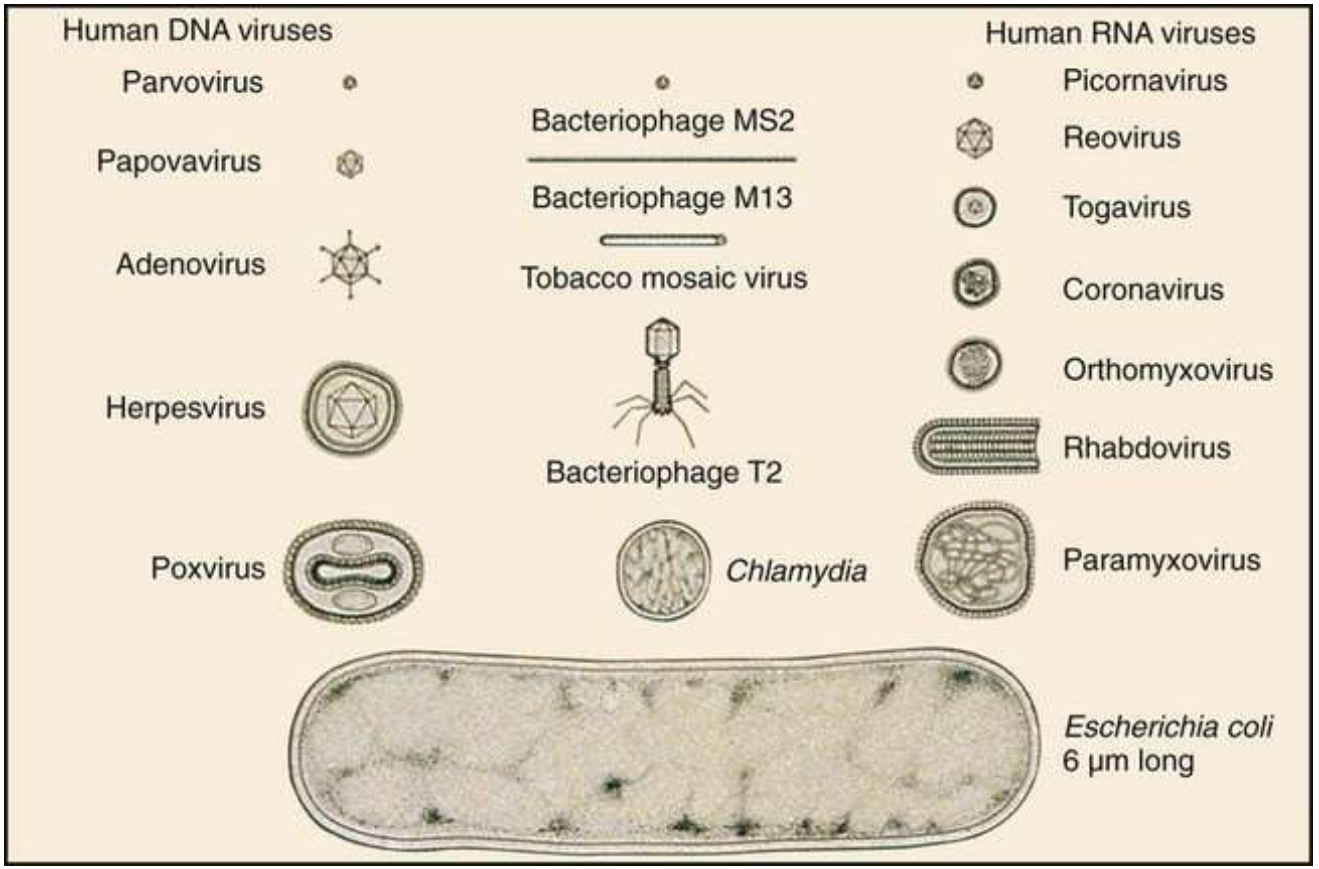
Gustav A. Kausche (1939)



Wendell M. Stanley (1941)

Molecular biology of pathogenic viruses

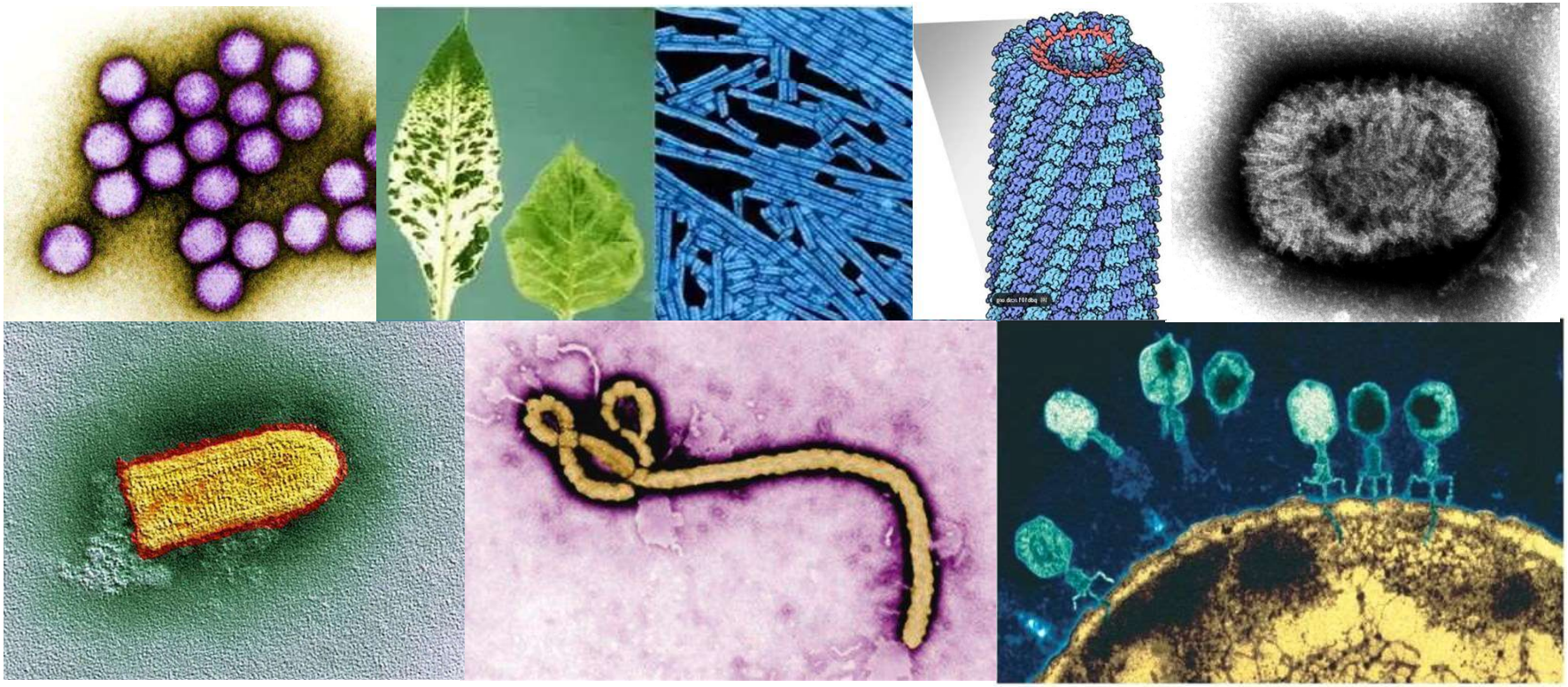
a small infectious agent that can only multiply inside living organisms by directing the host cell's machinery to generate more virus.



Most viruses vary in diameter from 20 nm to 250-400 nm.

The largest viruses measure about 500 nm in diameter and are about 700-1000 nm in length.

Molecular biology of pathogenic viruses

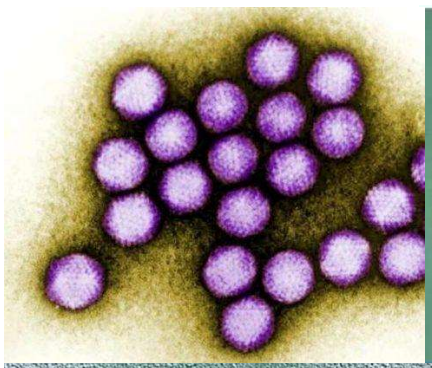


Molecular biology of pathogenic viruses

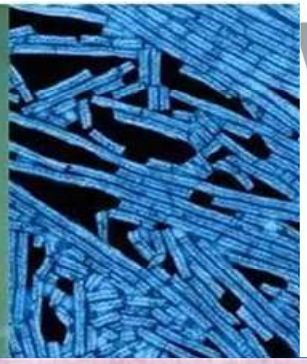
spherical: Adenovirus

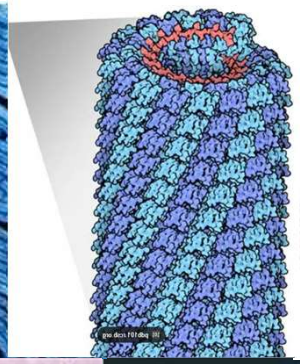
Rod-shaped helical: Tobacco mosaic virus

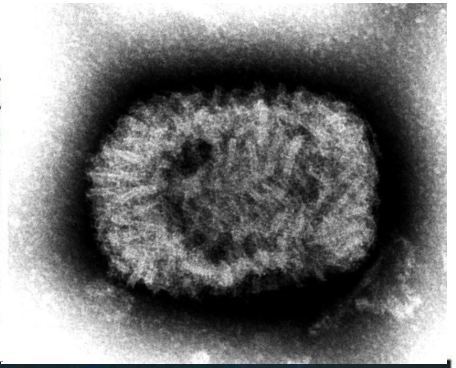
Brick-shaped: Variola virus (Smallpox Virus)

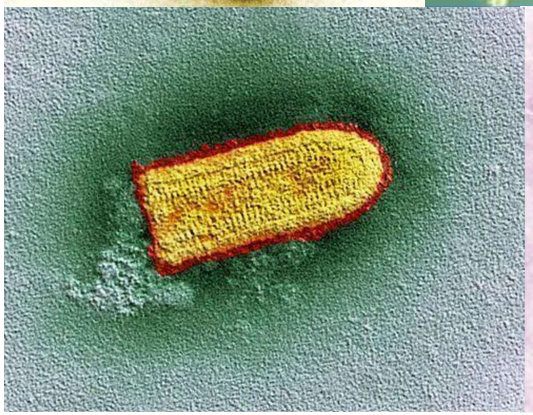




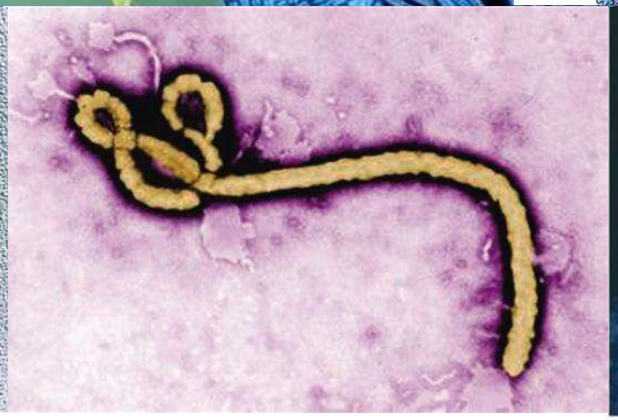








Bullet-shaped: Rhabdovirus



Cylindrical or tubular: Ebola virus

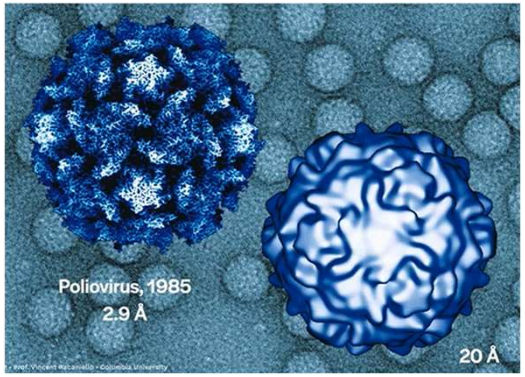


Complex: Bacteriophage M2

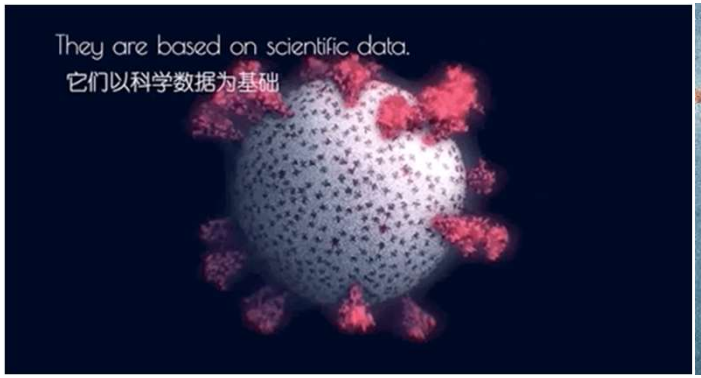
Molecular biology of pathogenic viruses

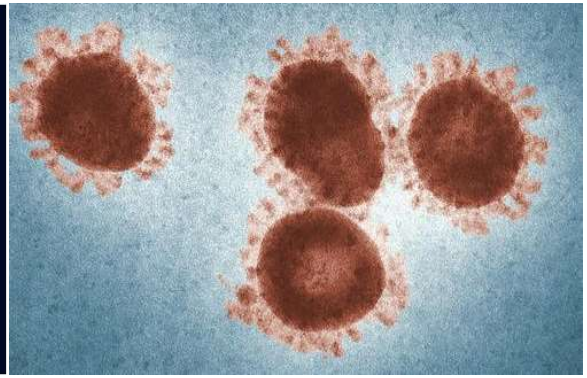
a small infectious agent that can only multiply inside living organisms by directing the host cell's machinery to generate more virus.

Naked/nonenveloped virus



envelope virus



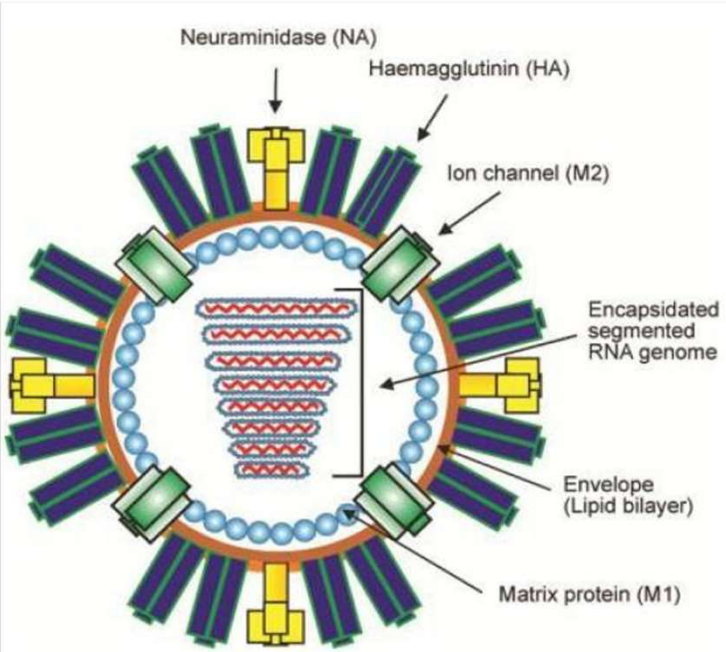


Molecular biology of pathogenic viruses

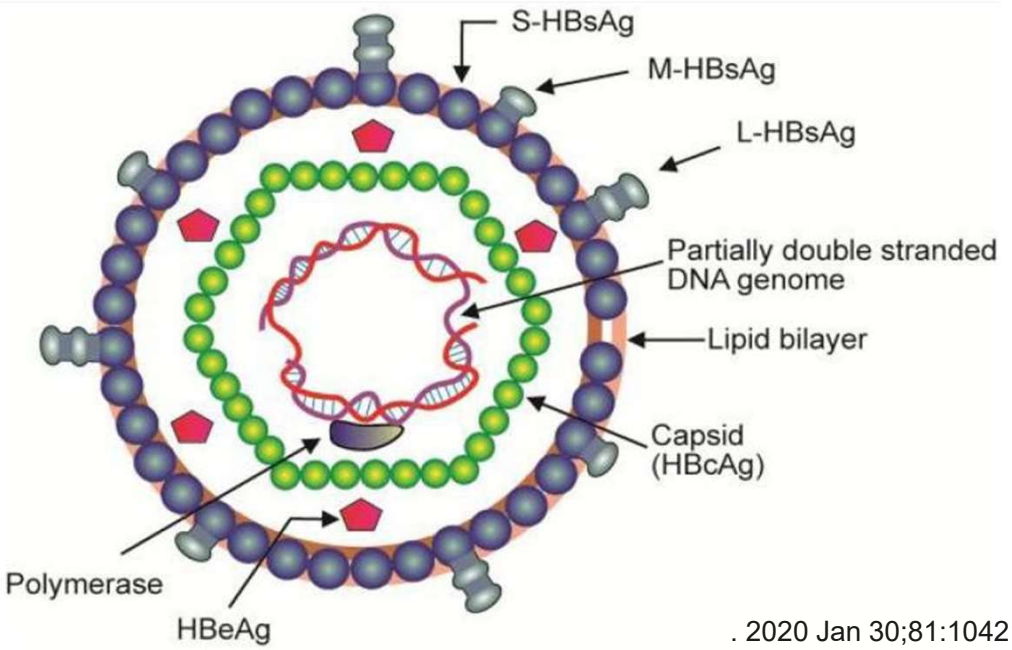
a small infectious agent that can only multiply inside living organisms by directing the host cell's machinery to generate more virus.

The genetic material of a virus is either RNA or DNA → RNA virus or DNA virus

influenza A virus

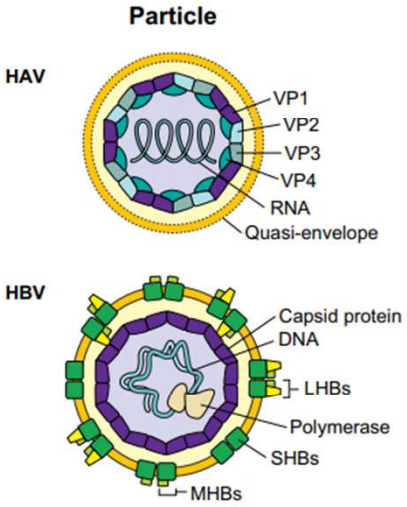


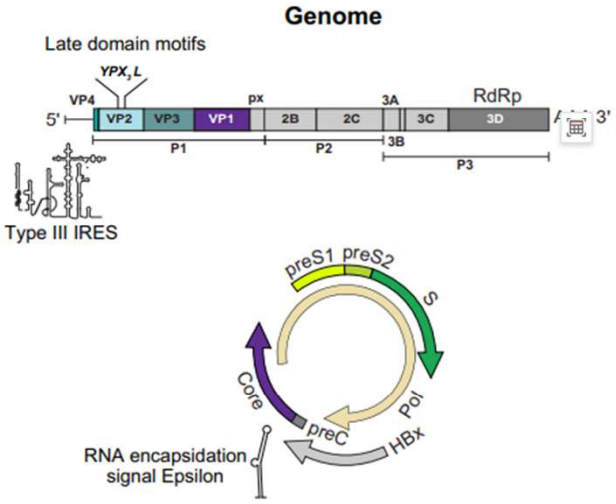
hepatitis B virus

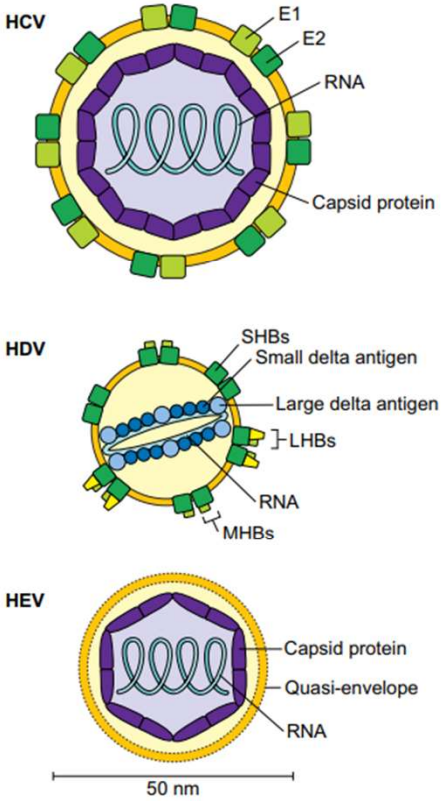


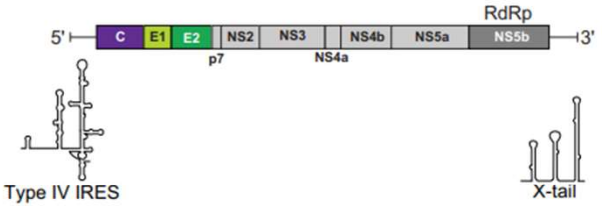
. 2020 Jan 30;81:104215.

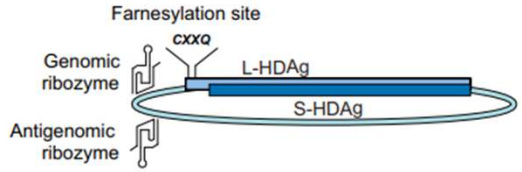
Molecular biology of human hepatitis viruses

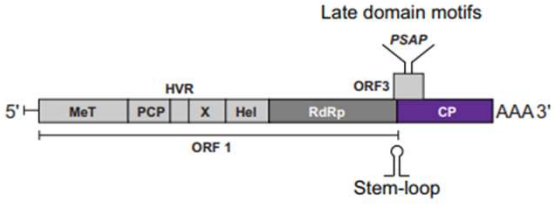












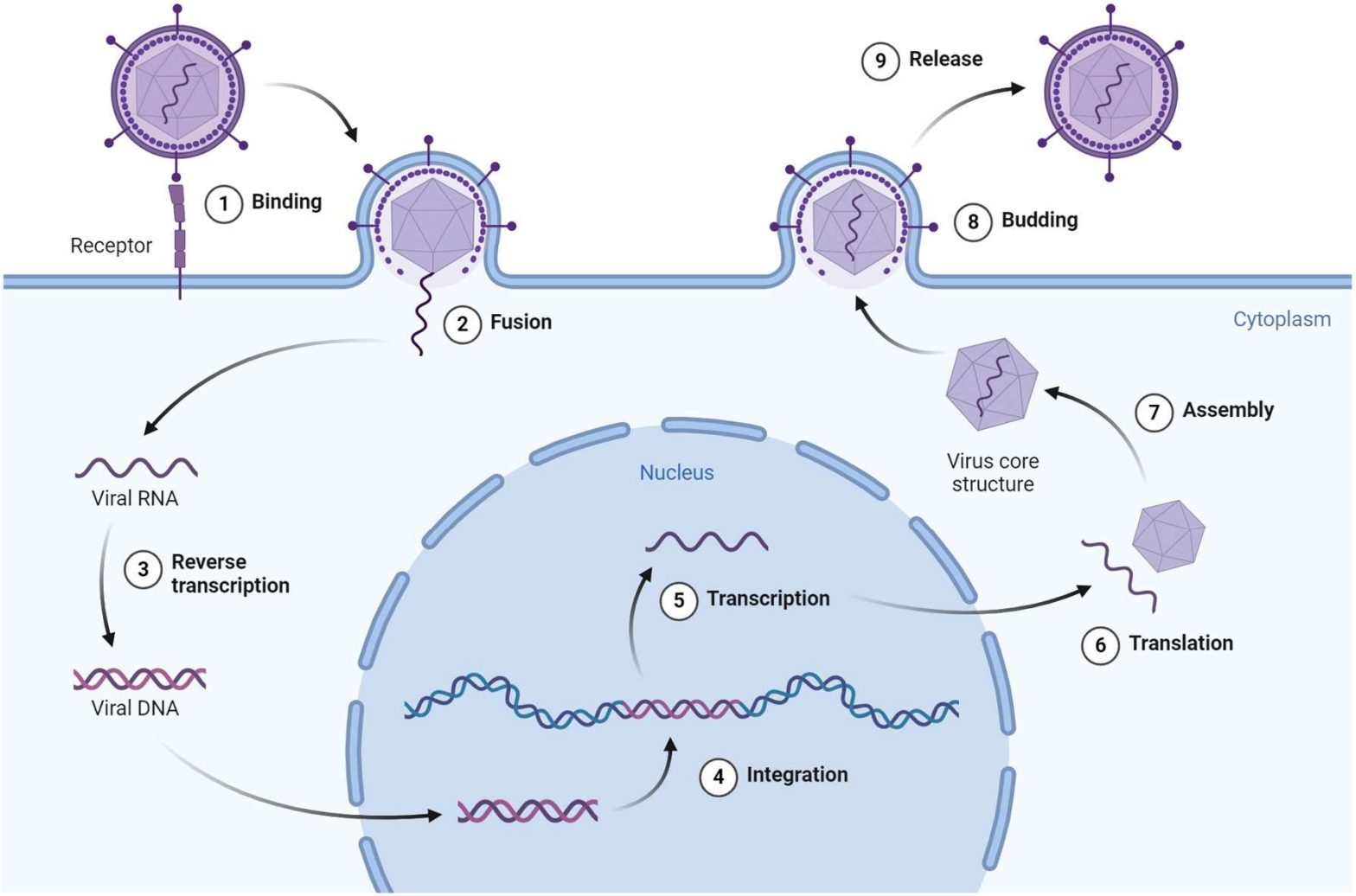
Properties of human hepatitis viruses

	HAV	HBV	HCV	HDV	HEV
Virus family, genus	*Picornaviridae*, *Hepatovirus*	*Hepadnaviridae*, *Orthohepadnavirus*	*Flaviviridae*, *Hepacivirus*	Unassigned, *Deltavirus*	*Hepeviridae*, *Orthohepevirus*
Genome type	Positive-sense linear ssRNA	Circular, partially dsDNA (full length negative-sense, partial positive-sense), replication via reverse transcription	Positive-sense linear ssRNA	Viroid-like, negative-sense circular ssRNA	Positive-sense linear ssRNA
Approx. genome length (nt)	7,500	3,200	9,600	1,700	7,200
Virion diameter (nm)	27–32	42	55–65	36–43	30–34
Envelope	No/quasi-enveloped	Yes	Yes	Yes	No/quasi-enveloped
Course of infection	Acute[61]	Acute/chronic (children 30–90%; adults <5%)[62]	Acute/chronic (80–85%)[63]	Acute/chronic (>80% if superinfection)[64]	Acute/chronic (<1%)[65]
Predominant transmission routes	Mainly faecal-oral, parenteral	Vertical, parenteral, sexual	Parenteral	Parenteral, sexual	Faecal-oral, food-borne, parenteral
Cellular receptor	Unknown[66]	NTCP, heparan sulfate proteoglycans[67,68]	CD81, SR-B1, LDL receptor, claudin-1, occludine[69–71]	NTCP, heparan sulfate proteoglycans[67,72]	Unknown

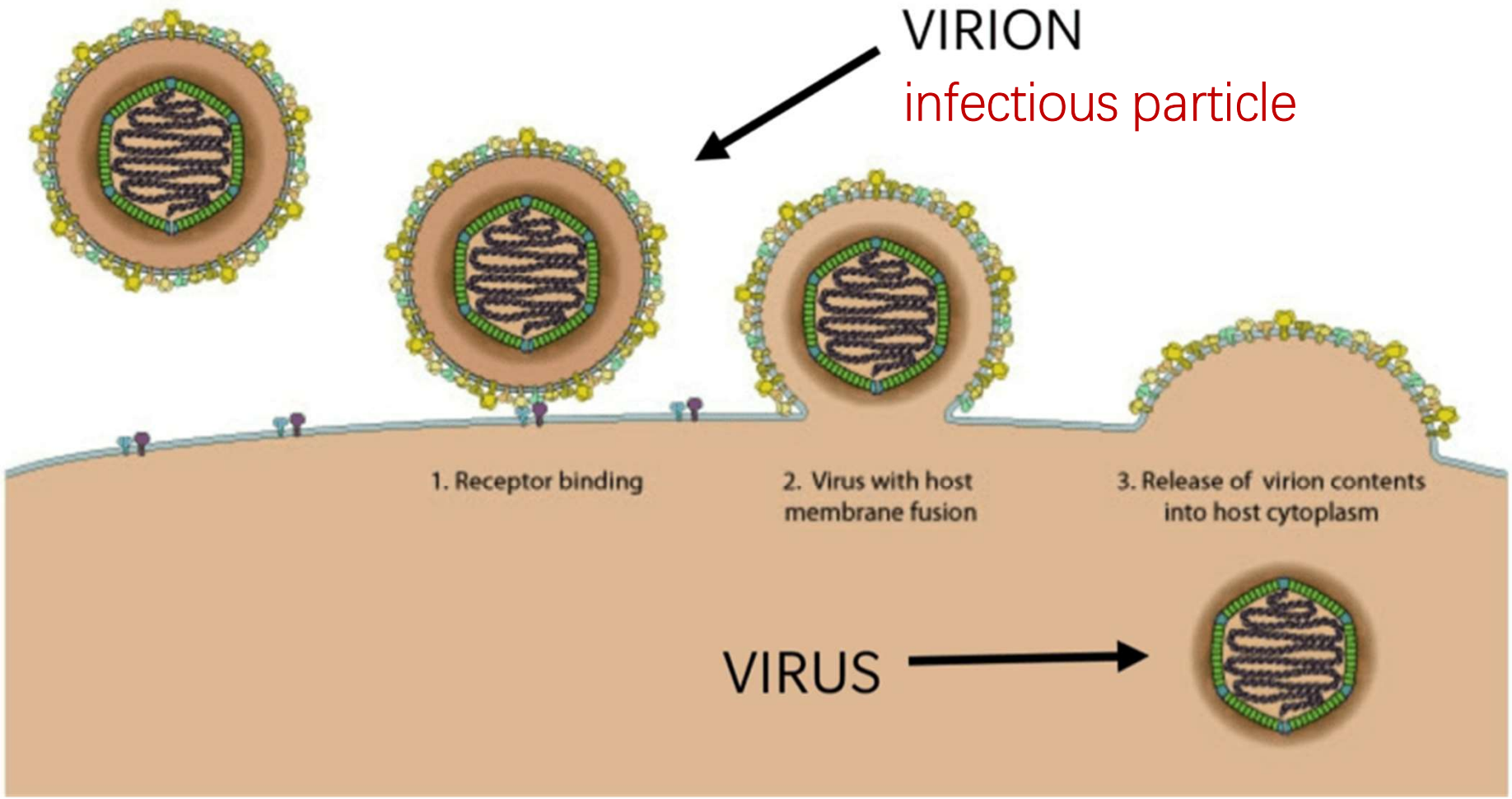
dsDNA, double-stranded DNA; nt, nucleotide; NTCP, sodium taurocholate co-transporting polypeptide; ssRNA, single-stranded RNA.

BioRender Disease Mechanisms – Infectious Diseases

Generic Viral Life Cycle



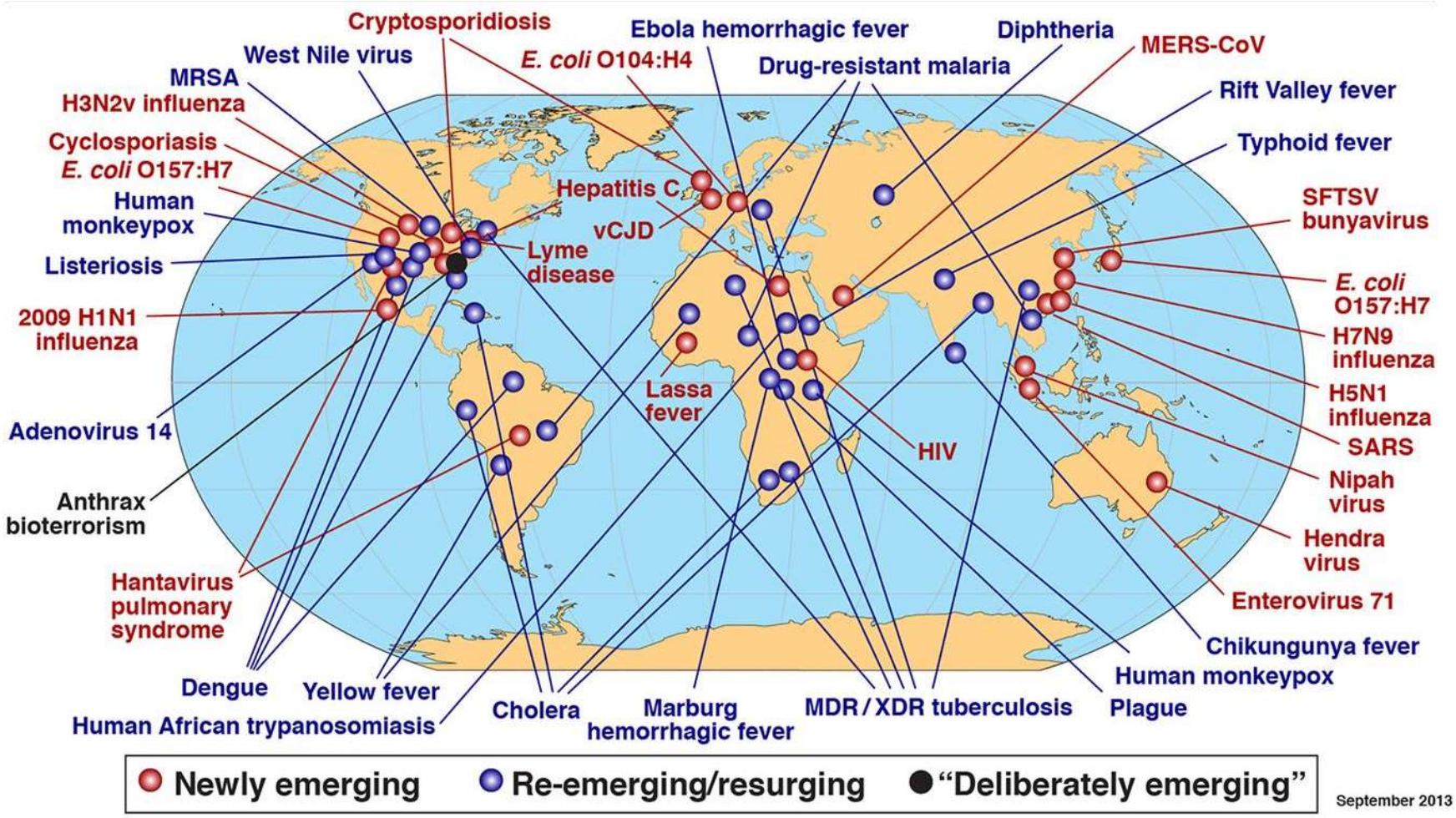
an organism with two phases



Discussion

- When do you know you get a VIRAL infectious disease?
- Any indicator? How to confirm?
- Do you know any molecular detection method?

frequent outbreaks of emerging and re-emerging infectious diseases



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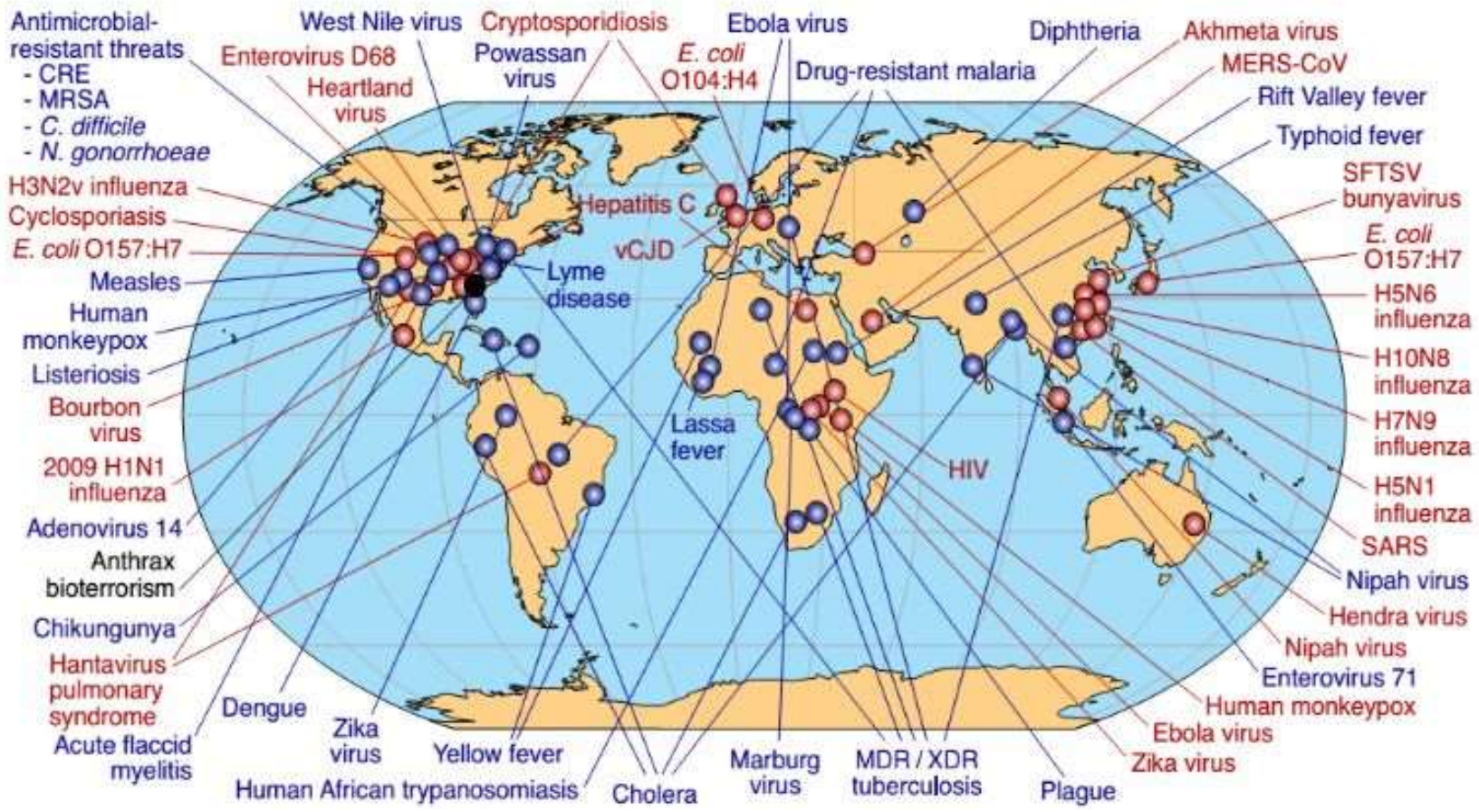
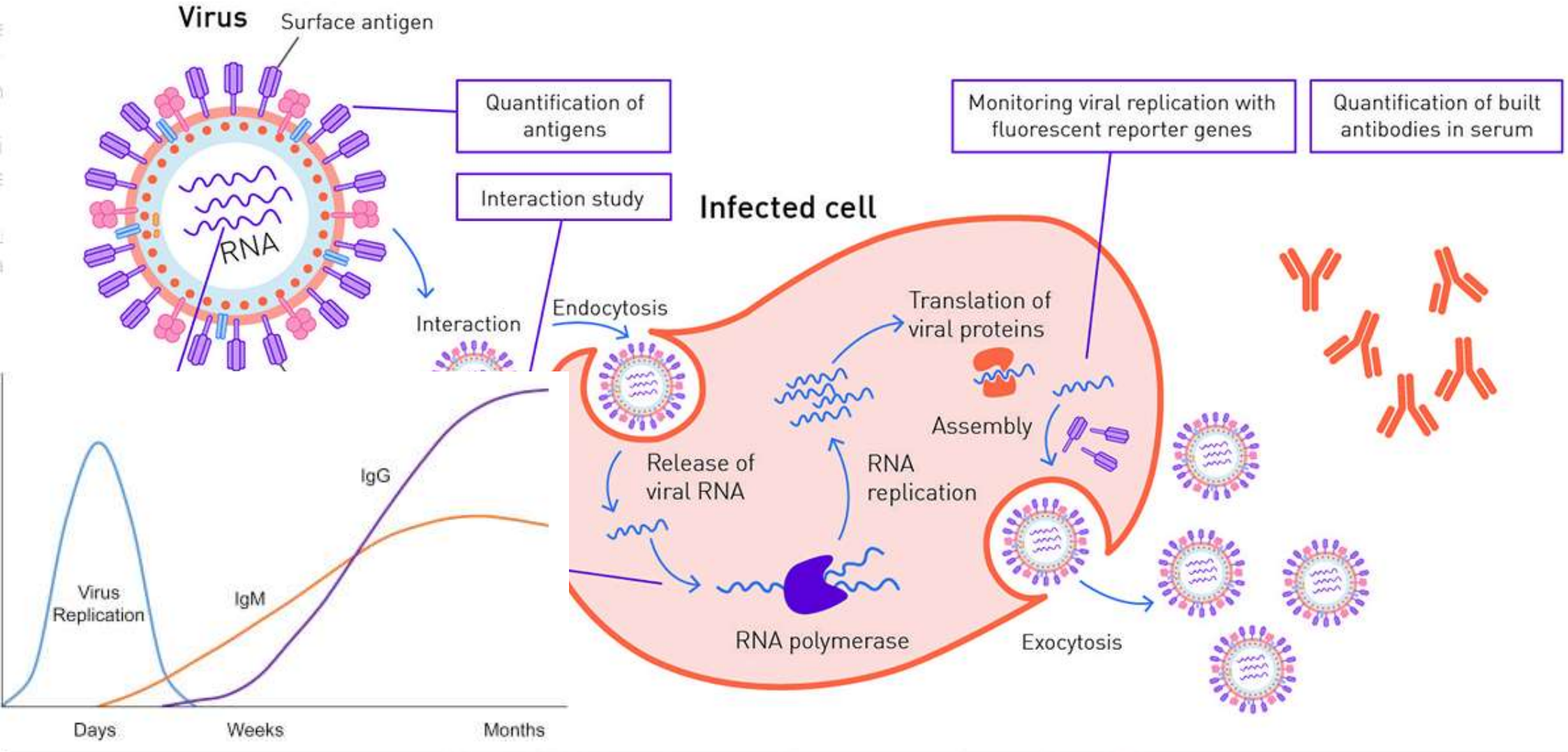


Viral life cycle in host cell and possible targets for detection methods



Diagnosis of Infectious Disease

Many different types of laboratory tests can identify microorganisms.

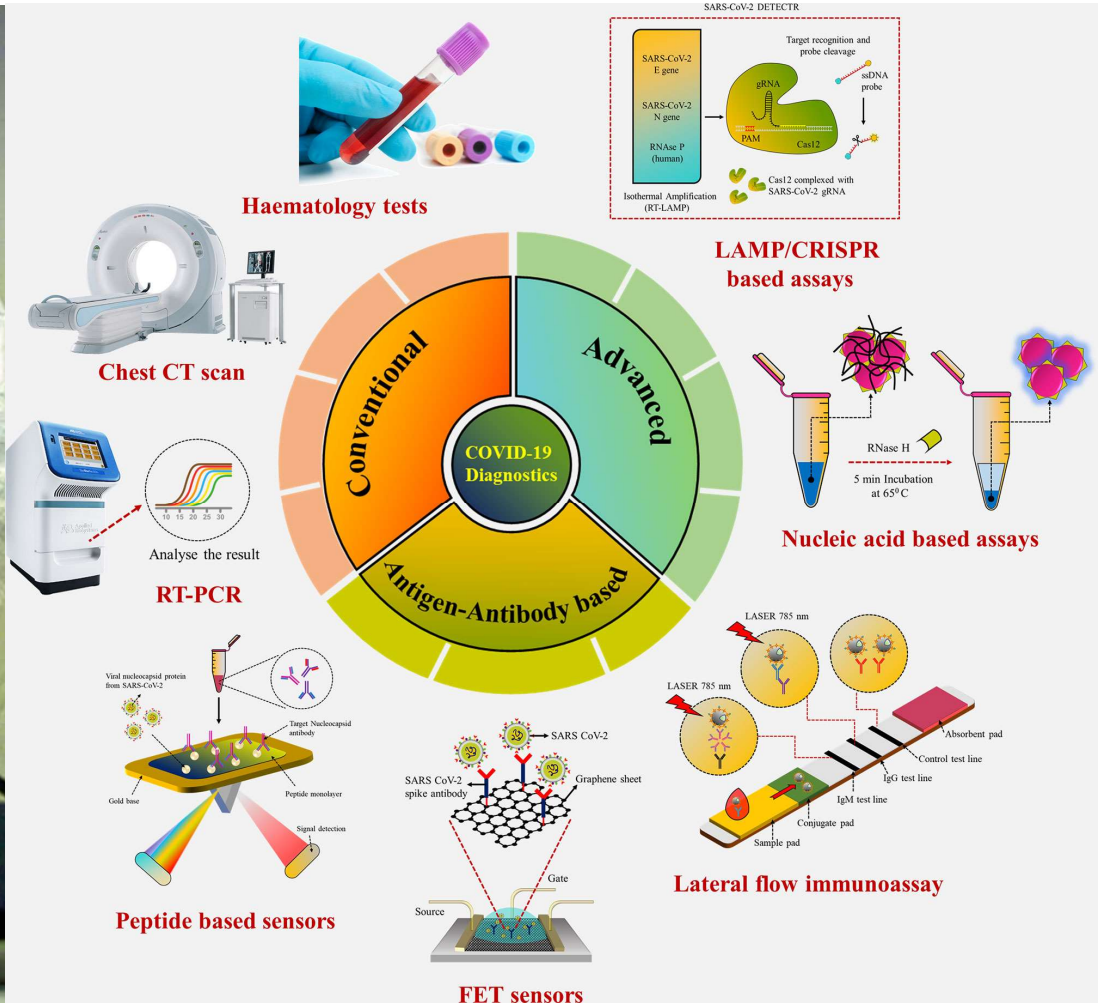
Laboratory tests use a sample of blood, urine, sputum, or other fluid or tissue from the body.

- Stained and examined under a microscope
- Cultured (placed in conditions that encourage the growth of microorganisms)
- Tested for antibodies (molecules produced by the person's immune system in response to the microorganism)
- Tested for a microorganism's antigens (molecules from the microorganism that can trigger an immune response in the body)
- Tested for genetic material (such as DNA or RNA) from the microorganism

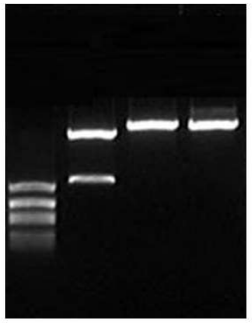
No single test can identify every microorganism!

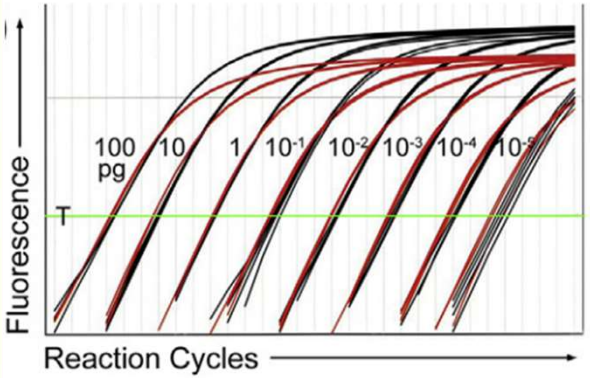
SARS 10 years later: How has the health care system changed?







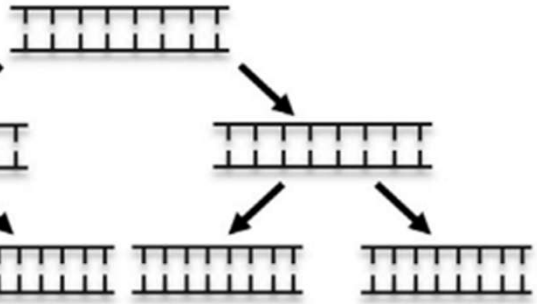




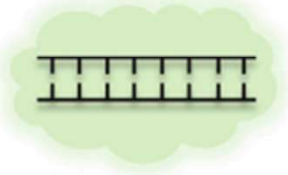


Regions on DNA viruses may be directly amplified. RNA viruses must undergo reverse transcription prior to amplification.

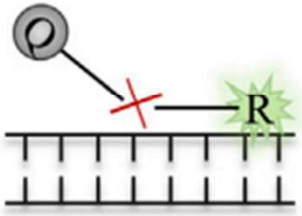
The target gene region is amplified exponentially by PCR.



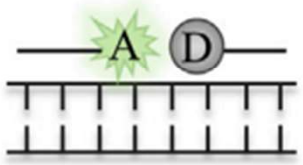
The use of probes and dyes are among the most popular methods for monitoring target amplification.



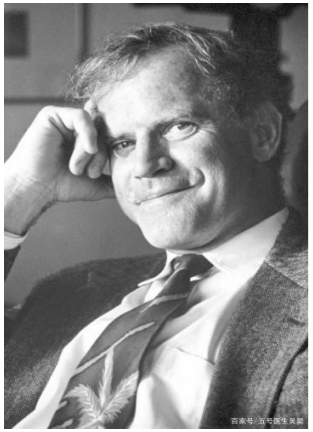
Dyes intercalate with double stranded DNA to produce measurable fluorescence.



Hydrolysis probes fluoresce upon cleavage of the quencher away from the reporter during amplification.

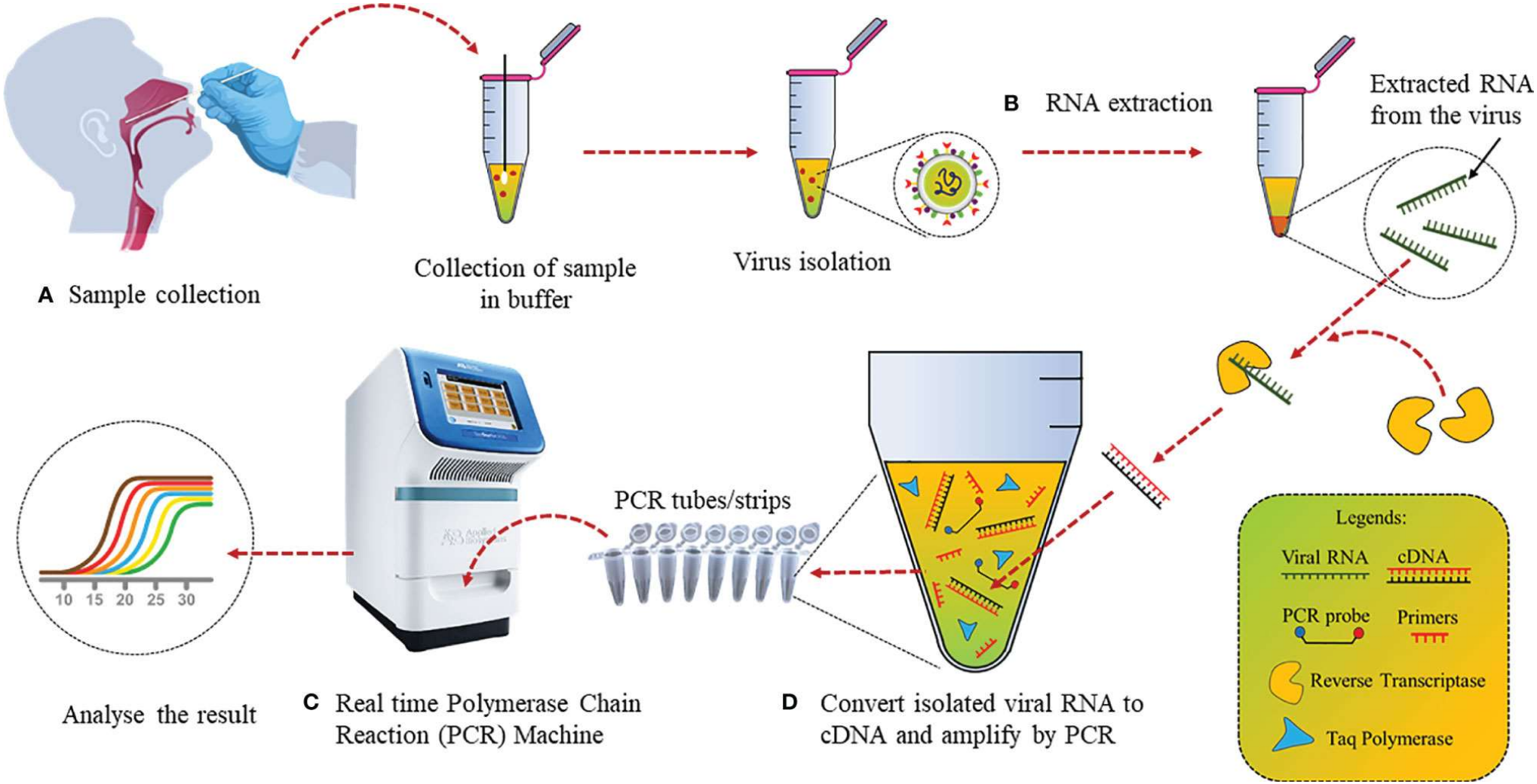


Hybridisation probes bind the target to bring acceptor and donor fluorophores into close proximity, permitting fluorescence.

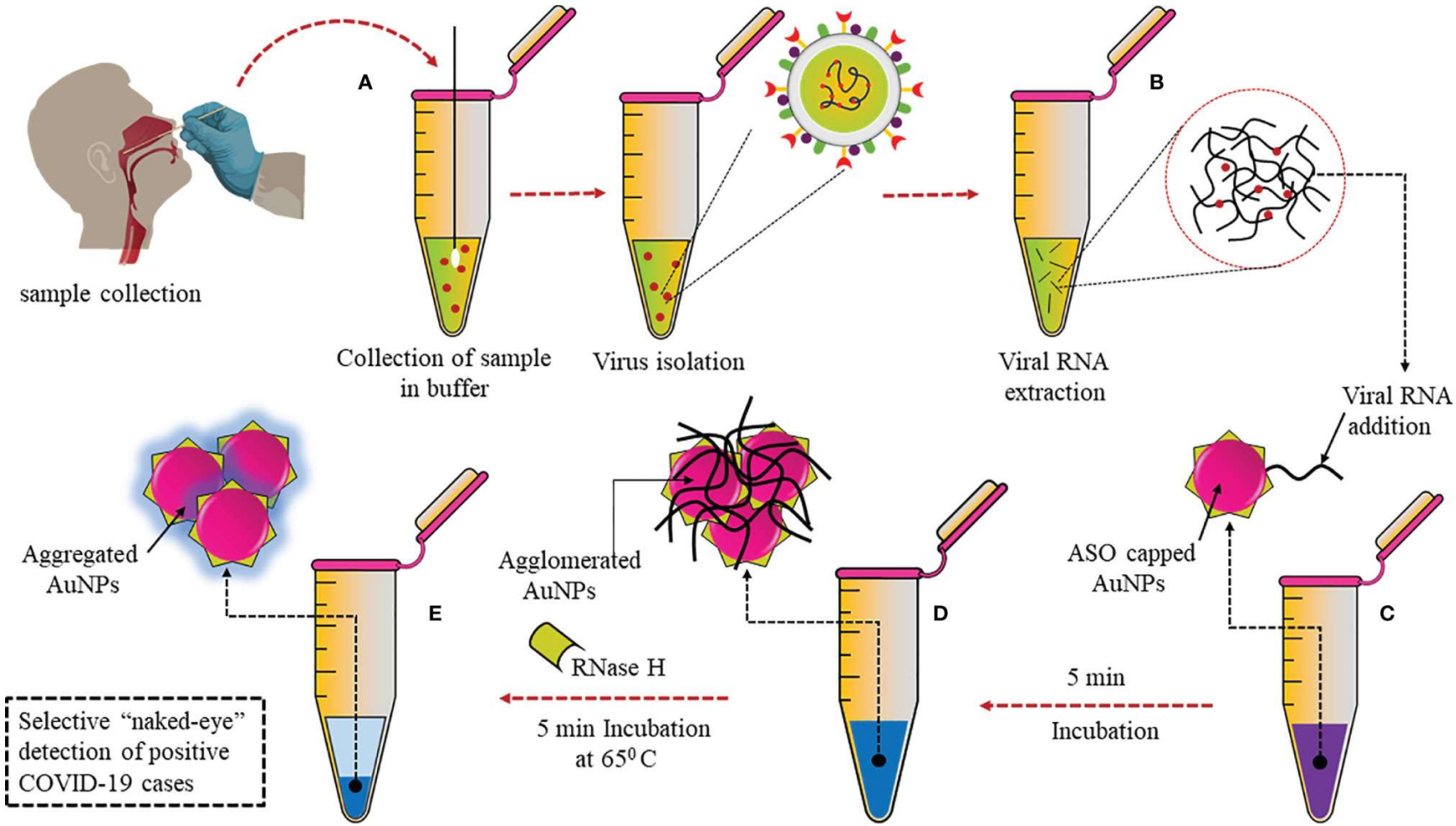


Kary Banks Mullis

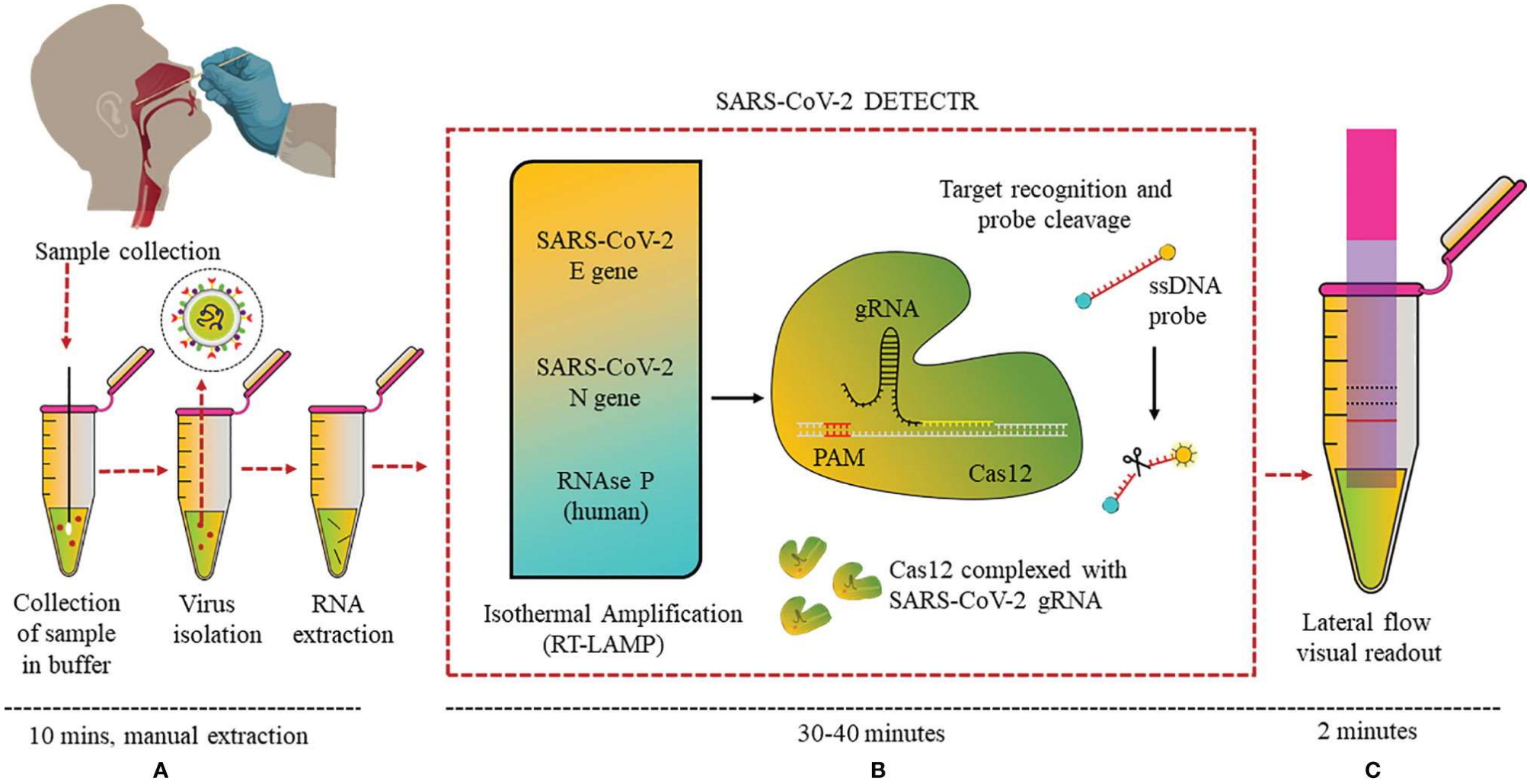
Detection of SARS-CoV-2 by conventional RT-PCR



Selective naked eye SARS-CoV-2 detection



Selective naked eye SARS-CoV-2 detection



Take home messages

- Virus is a small infectious agent that can only multiply inside living organisms.
- >50% emerging and re-emerging infectious diseases are caused by virus.
- Efficient diagnosis helps to track and control pandemic outbreaks.
- Many different types of laboratory tests can identify virus infections.
- No single test can identify every virus.